

In the Specification:

Please amend the specification as shown:

Please delete the paragraphs on page 14, line 8 to page 15, line 17 and replace them with the following paragraphs:

Generally, said domain (A) is not directly fused to said domain (B) since it may be advantageous to introduce between them a spacer (peptide sequence which allows for separating said domains (A) and (B) from each other). Therefore, if desired, the gene construction of the invention may contain, in addition, a fourth nucleic acid sequence encoding a spacer placed between said second and third nucleic acid sequences, wherein the 5' end of said fourth nucleic acid sequence is linked to the 3' end of said second nucleic acid sequence and the 3' end of said fourth nucleic acid sequence is linked to the 5' end of said third nucleic acid sequence. Thus, the nucleotide sequence encoding the single-domain recombinant antibody or antibodies is joined to the nucleotide sequence encoding the C-terminal domain of an AT by means of a nucleotide sequence encoding a spacer. Advantageously, said spacer is a peptide sequence having structural flexibility (i.e., flexible). Practically any peptide sequence having structural flexibility may be used. Said flexible peptide sequence may comprise, for example, multimers or repetitions of amino acid residues, such as, alanine (A), glycine (G), etc., the peptide sequence –AAAAGA- (SEQ ID NO: 11) or any other suitable non repetitive sequence of amino acid residues such as, for example, the non repetitive spacer of sequence –TPSHNSHQVPSAGGPTANS- (SEQ ID NO: 12) (one-letter code of amino acids), etc., or the hinge region of an antibody.

When the hybrid protein provided by the instant invention as a result of the expression of the nucleic acid sequence contained in the gene construction of the invention comprises two or more single-domain recombinant antibodies, said antibodies may be, optionally, separated from each other by spacers of the previously defined type, so that said single-domain recombinant antibodies are not directly fused between them but through said spacers. Therefore, if desired, the gene construction of the invention may further contain a nucleic acid sequence encoding a spacer placed between two nucleic acid sequences encoding said single-domain recombinant antibodies. Thus, the nucleotide sequences encoding the single-domain recombinant antibodies are joined to each other by a nucleotide sequence encoding a spacer. The same spacer used for separating the domains (A) and (B), previously defined, may be used for separating the single-domain recombinant antibodies from each other. In a particular embodiment, the spacer used is the non repetitive spacer of sequence –TPSHNSHQVPSAGGPTANS- (SEQ ID NO: 12) (one-letter code of amino acids) (Example 1, A48 constructions and V_{amy} repetitions).

Please delete the paragraphs on page 24, lines 6-32 and replace them with the following paragraphs:

1.2 Construction of the C-IgAP and 2V_{amy} hybrid protein (2V_{amy}β)

An approximately 0.4 kb DNA fragment encoding V_{amy} was amplified by PCR using the Linker-A48-V_{amy}A (SEQ ID NO: 5) and V_{amy}-Not (SEQ ID NO: 6) primers of the phagemid A100R3A2 (see 1.1 above). The V_{amy} fragment was bound to the oligonucleotide Linker-A48 (SEQ ID NO: 7), which encodes the scFv A48III-1 flexible peptide (Proba et al., J. Mol. Biol. 1998, 275(2): 245-253), by a PCR reaction without primers, due to the homology between the first 24 bases of the Linker-A48-V_{amy}A and Linker-A48. This reaction was used for the amplification of the Linker-V_{amy} fusion product, using the oligonucleotides V_{amy}-Not (SEQ ID NO: 6) and Linker-A48-V_{amy}-eagI (SEQ ID NO: 8) as primers. The obtained PCR product (Linker-V_{amy}) was digested with NotI and cloned into plasmid pV_{amy}β digested with the same enzyme. The new plasmid p2V_{amy}β encodes for a hybrid protein made up of two V_{HH} (V_{amy}β) bound by a flexible linker and fused to the C-IgAP. The amino acid sequence of said flexible linker is –TPSHNSHQVPSAGGPTANS~~G~~- **(SEQ ID NO: 12)** (amino acid one-letter code).

1.3 Construction of the C-IgAP and 3V_{amy} hybrid protein (3V_{amy}β)

The product of the previous PCR reaction (Linker-V_{amy}) was digested with NotI and cloned into p2V_{amy}β digested with NotI. The new plasmid, called p3V_{amy}β, encoded a hybrid protein made up of three V_{HH} (V_{amy}β) bound by a flexible linker and fused to the C-IgAP. The amino acid sequence of said flexible linker is –TPSHNSHQVPSAGGPTANS~~G~~- **(SEQ ID NO: 12)** (amino acid one-letter code).